

COVER LETTER

Principal Investigator: John D. Chodera

Application Title: The role of reorganization energy in achieving selective kinase inhibition

Funding Opportunity: R01 (PA-16-160)

Please assign this application to the following:

Institute: NIGMS

Scientific Review Group: Biological Chemistry and Macromolecular Biophysics IRG [BCMB]

This study focuses on a combined computational and experimental investigation of the contribution of conformational reorganization energy to small molecule kinase inhibitor selectivity and the potential for exploiting this phenomena to develop new selective molecules. We utilize a variety of techniques, including massively distributed biomolecular simulations, kinetic modeling of biomolecular dynamics, alchemical free energy calculations of ligand binding energetics, and automated biophysical measurements.